What is claimed is:

1. An assay for identifying compounds having potential *hedgehog* bioactivity, comprising:
   (a) forming a reaction mixture including:
      (i) a *hedgehog* polypeptide,
      (ii) a *patched* polypeptide, and
      (iii) a test compound; and
   (b) detecting interaction of the *hedgehog* and *patched* polypeptides;
   wherein a statistically significant change in the interaction of the *hedgehog* and *patched* polypeptides in the presence of the test compound, relative to the interaction in the absence of the test compound, indicates a potential *hedgehog* activity for the test compound.

2. The assay of claim 1, wherein the reaction mixture is a cell-free protein preparation.

3. The assay claim 1, wherein the reaction mixture comprises a recombinant cell including a heterologous nucleic acid recombinantly expressing the *patched* polypeptide.

4. The assay of claim 1, wherein the step of detecting interaction of the *hedgehog* and *patched* polypeptides comprises a competitive binding assay.

5. The assay of claim 3, wherein the step of detecting interaction of the *hedgehog* and *patched* polypeptides comprises detecting change in the level of an intracellular second messenger responsive to signaling by the *patched* polypeptide.

6. The assay of claim 3, wherein the step of detecting interaction of the *hedgehog* and *patched* polypeptides comprises detecting change in the level of expression of a gene controlled by a transcriptional regulatory sequence responsive to signaling by the *patched* polypeptide.

7. The assay of claim 3 wherein the recombinant cell substantially lacks expression of an endogenous *patched* protein.

8. An assay for screening test compounds to identify agents which modulate the binding of *hedgehog* proteins with a *hedgehog* receptor, comprising:
   i. combining, as a cell-free system, a *hedgehog* polypeptide, a *hedgehog* receptor polypeptide, and a test compound; and

ii. detecting formation of a complex comprising the *hedgehog* and receptor polypeptides,

wherein a statistically significant change in the formation of the complex in the presence of the test compound is indicative of an agent that modulates interaction between *hedgehog* proteins with a cognate *hedgehog* receptor.

9. The assay of claim 8, wherein the cell-free system is a cell membrane preparation.

10. The assay of claim 8, wherein the cell-free system is a reconstituted protein mixture.

11. The assay of claim 8, wherein the cell-free system is a liposome reconstituting the receptor polypeptide as a *hedgehog* receptor.

12. The assay of claim 8, wherein at least one of the *hedgehog* polypeptide and the receptor polypeptide comprises a detectable label, and interaction of the *hedgehog* and receptor polypeptides is quantified by detecting the label in the complex.

13. The method of claim 12, wherein the detectable label is selected from the group consisting of radioisotopes, fluorescent compounds, enzymes, and enzyme co-factors.

14. The assay of claim 8, wherein the complex is detected by an immunoassay.

15. The assay of claim 8, wherein the receptor is a *patched* polypeptide.

16. The assay of claim 8, further comprising the step of contacting the compound, which produced statistically significant change in the formation of the complex, with a cell expressing a *hedgehog* receptor and determining if the compound can cause a phenotypic change in the cell.

17. An assay for screening test compounds to identify agents which modulate the binding of *hedgehog* proteins with a *hedgehog* receptor, comprising:

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i. providing a cell expressing a *hedgehog* receptor;

ii. contacting the cell with a *hedgehog* polypeptide and a test compound; and

iii. detecting interaction of the *hedgehog* polypeptide and receptor,

wherein a statistically significant change in the level of interaction of the *hedgehog* polypeptide and receptor is indicative of an agent that modulates the interaction of *hedgehog* proteins with a *hedgehog* receptor.

18. The assay of claim 17, wherein the interaction of the *hedgehog* polypeptide and receptor is detected by detecting change in phenotype of the cell relative to the absence of the test compound.

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19. The assay of claim 17, wherein the change is phenotype is detected by detecting gain or loss of expression of a cell-type specific marker.

20. The assay of claim 17, wherein the receptor transduces a signal in the cell which is sensitive to *hedgehog* binding, and the cell further comprises a reporter gene construct comprising a reporter gene in operable linkage with a transcriptional regulatory sequence sensitive to intracellular signals transduced by interaction of the *hedgehog* polypeptide and receptor, expression of the reporter gene providing a detectable signal for detecting interaction of the *hedgehog* polypeptide and receptor.

21. The assay of any of claims 20 or 33, wherein the reporter gene encodes a gene product that gives rise to a detectable signal selected from the group consisting of: color, fluorescence, luminescence, cell viability relief of a cell nutritional requirement, cell growth, and drug resistance.

22. The assay of claim 21, wherein the reporter gene encodes a gene product selected from the group consisting of chloramphenicol acetyl transferase, luciferase, beta-galactosidase and alkaline phosphatase.

23. The assay of claim 20, wherein the reporter gene includes a transcriptional regulatory sequence of a gene selected from the group consisting of a GLI gene and *patched* gene.

24. The assay of claim 17, wherein the receptor transduces a signal in the cell which is sensitive to *hedgehog* binding, and interaction of the *hedgehog* polypeptide and receptor are detected by detecting change in the level of an intracellular second messenger responsive to signaling by the receptor.

25. The assay of claim 24, wherein the interaction of the *hedgehog* polypeptide and receptor is detected by changes in intracellular protein phosphorylation.

26. The assay of claim 17, wherein the receptor is a *patched* receptor.

27. The assay of any of claims 17 and 26, wherein the cell further comprises a heterologous gene construct encoding the receptor.

28. The assay of claim 17, wherein the step of detecting interaction of the *hedgehog* polypeptide and receptor comprises a competitive binding assay.

29. The assay of claim 17, wherein the cell further comprises one or more heterologous gene constructs encoding *costal-2*, *fused* and/or *smoothened* genes, or homologs thereof.

30. An assay for screening test compounds to identify agents which modulate the activity of a mammalian *patched* protein, comprising:

i. providing a cell expressing a recombinant mammalian *patched* protein;

ii. contacting the cell with a test compound; and

iii. detecting an effect, if any, of the test compound on signal transduction by the *patched* protein,

wherein a statistically significant change in the signal transduction of *patched* in the presence of the test compound, relative to the absence of the test compound or absence of the *patched* protein, is indicative of an agent that modulates the activity of *patched* protein.

31. The assay of claim 30, wherein the signal transduction by the *patched* protein is detected by detecting change in phenotype of the cell relative to the absence of the test compound.

32. The assay of claim 30, wherein the *patched* protein is recombinantly expressed in the cell.

33. The assay of claim 30, wherein the cell further comprises a reporter gene construct comprising a reporter gene in operable linkage with a transcriptional regulatory sequence sensitive to intracellular signals transduced by interaction of a *hedgehog* polypeptide with the *patched* protein, expression of the reporter gene providing a detectable signal for detecting signal transduction by the *patched* protein.

34. The assay of any of claims 1, 15, 26 or 30, wherein the *patched* polypeptide is of vertebrate origin.

35. The assay of claim 34, wherein the *patched* polypeptide is of mammalian origin.

36. The assay of claim 35, wherein the *patched* polypeptide is human *patched* protein.

37. The assay of claim 36, wherein the *patched* polypeptide is a recombinant polypeptide.

38. The assay of any of claims 1, 8 or 17, wherein the *hedgehog* polypeptide is of vertebrate origin.

39. The assay of claim 38, wherein the *hedgehog* polypeptide is of mammalian origin.

40. The assay of claim 38, wherein the *hedgehog* polypeptide is human *hedgehog* protein.

41. The assay of any of claims 1, 8 or 17, wherein the *hedgehog* polypeptide is a recombinant polypeptide.

42. The assay of any of claims 3, 17 or 30, wherein the recombinant cell is a metazoan cell.

43. The assay of claim 42, wherein the recombinant cell is a mammalian cell.

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44. The assay of claim 42, wherein the recombinant cell is an insect cell.

45. The assay of any of claims 3, 17 or 30, wherein the recombinant cell is a oocyte.

46. The assay of any of claims 3, 17 or 30, wherein the recombinant cell is a yeast cell.

47. The assay of any of claims 1, 8, 17 or 30, wherein the steps of the assay are repeated for a variegated library of at least 100 different test compounds.

48. The assay of any of claims 1, 8, 17 or 30, wherein the test compound is selected from the group consisting of small organic molecules, and natural product extracts.

49. The assay of any of claims 1, 8, 17 or 30, further comprising a step of preparing a pharmaceutical preparation of one or more compounds identified.

50. A recombinant cell, comprising:

(i) an expressible recombinant gene encoding a heterologous *patched* polypeptide whose signal transduction activity is modulated by binding to a *hedgehog* protein; and

(ii) a reporter gene construct containing a reporter gene in operative linkage with one or more transcriptional regulatory elements responsive to the signal transduction activity of the cell *patched* polypeptide.

51. The cell of claim 50, wherein the *patched* polypeptide is of vertebrate origin.

52. The cell of claim 51, wherein the *patched* polypeptide is of mammalian origin.

53. The cell of claim 52, wherein the *patched* polypeptide is human *patched* protein.

54. The cell of claim 50, which cell substantially lacks expression of an endogenous *patched* protein.

55. The cell of claim 50, which cell is a metazoan cell.

56. The cell of claim 55, which cell is a mammalian cell.

58. The cell of claim 50, wherein the reporter gene encodes a gene product that gives rise to a detectable signal selected from the group consisting of: color, fluorescence, luminescence, cell viability relief of a cell nutritional requirement, cell growth, and drug resistance.

59. The cell of claim 47, wherein the reporter gene encodes a gene product selected from the group consisting of chloramphenicol acetyl transferase, luciferase, beta-galactosidase and alkaline phosphatase.

60. The cell of claim 50, wherein the reporter gene includes a transcriptional regulatory sequence of a gene selected from the group consisting of a GLI gene and *patched* gene.

61. A kit for screening test compounds to identify agents which modulate the binding of *hedgehog* proteins with a *hedgehog* receptor, comprising a cell of claim 50 and a preparation of purified *hedgehog* polypeptide.

62. An assay for identifying compounds which inhibit the proteolytic activity of a *hedgehog* protein, comprising:

(a) forming a reaction mixture including:

(i) a *hedgehog* protein having an endogenous proteolytic activity,

(ii) a substrate for the *hedgehog* proteolytic activity, and

(iii) a test compound; and

(b) determining the rate of conversion of the substrate to product by the *hedgehog* proteolytic activity;

wherein a statistically significant decrease in the rate of substrate conversion in the presence of the test compound, relative to the absence of the test compound, indicates a that the test compound is an inhibitor of the proteolytic activity of the *hedgehog* protein.

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